IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:
Yi Feng Zheng, *et al.*

Serial No.: 10/736,004

Confirmation No.: 2953

Filed: December 15, 2003

Title: Assays for Entactogens

Board of Patent Appeals and Interferences
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPELLANT'S BRIEF ON APPEAL

This is an appeal from the Final Rejection in the Office Action dated January 24, 2007 (the "Final Rejection"), by the United States Patent and Trademark Office (the "Office") in the above-identified patent application. A Notice of Appeal was filed electronically on May 22, 2007.

Jurisdiction over this appeal resides in the Board of Patent Appeals and Interferences under 35 U.S.C. §134.

An oral hearing was not requested.

REAL PARTY IN INTEREST

The real party in interest is Dade Behring Marburg GmbH.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

STATUS OF CLAIMS

The claims for consideration on appeal in the present application are Claims 25, 27, 30 and 31, which are all of the claims remaining in the present application. Claims 1-12, 14, 20, 22, 23, 26, 28, 29 and 32 were previously canceled in amendments filed prior to the final rejection and Claims 13, 15-19, 21 and 24 were canceled in an Amendment under 37 C.F.R. §41.33 filed on June 15, 2007. Claims 25, 27, 30 and 31 stand rejected.

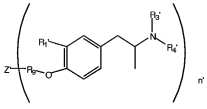
STATUS OF THE AMENDMENTS

An Amendment under 37 C.F.R. §41.33 was filed on June 15, 2007, canceling Claims 13, 15-19, 21 and 24. A Response under 37 C.F.R. 1.116 (the AF Response) was filed after the final rejection; no amendments were made in the AF Response. All amendments to the claims made prior to the final rejection have been entered and the claims set forth in the Claims Appendix represent the current state of the claims and include all entered amendments.

SUMMARY OF CLAIMED SUBJECT MATTER

Claim 25 is directed to a method for determining methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethylamphetamine in a sample suspected of containing methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethylamphetamine (p 26, ln 20-23, and p 27, ln 24-27, where p = page(s) and ln = line(s) of the specification). A combination is provided in a medium (p 26, ln 4). The

combination comprises: (i) the sample (p 26, ln 25), (ii) an antibody for methylenedioxyamphetamine (p 26, ln 26), and/or (iii) an antibody for methylenedioxymethamphetamine (p 26, ln 27), and/or (iv) an antibody for methylenedioxyethamphetamine (p 26, ln 28), and (v) a compound of the formula (p 26, ln 29, to p 27, ln 8, p 7, ln 29):



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is H, or methyl or ethyl,

R^{9} is $-(CH_2)_nC(O)$,

Z' is an enzyme,

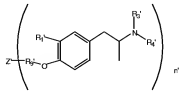
n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of the enzyme divided by about 500.

The medium is examined for the presence of a complex comprising the methylenedioxyamphetamine and the antibody for methylenedioxyamphetamine and/or a complex of the methylenedioxymethamphetamine and the antibody for methylenedioxymethamphetamine and/or a complex of the methylenedioxyethamphetamine and the antibody for methylenedioxyethamphetamine, the presence thereof indicating the presence of the methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in the sample (p 27, ln 9-16).

Claim 27 is directed to a method for determining methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in a sample suspected of containing methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine (p 28, ln 23-26). A combination is provided in a medium (p 28, ln 27). The combination comprises (i) the sample (p 28, ln 28), (ii) a conjugate of an enzyme and a methylenedioxyamphetamine analog and a conjugate of an enzyme and a methylenedioxymethamphetamine analog and a conjugate of an enzyme and a methylenedioxyethamphetamine

analog (p 28, ln 29-31), (iii) an antibody for methylenedioxyamphetamine, the antibody being raised against a compound of the formula (p 29, ln 1-13, and p 7, ln 29):



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is H,

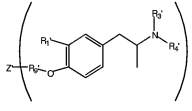
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of the protein immunogenic carrier or the non-poly(amino acid) immunogenic carrier divided by about 500; and

(iv) an antibody for methylenedioxymethamphetamine, the antibody being raised against a compound of the formula (p 29, ln 14-25, and p 7, ln 29):



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is methyl,

$R^{9'}$ is $-(CH_2)_nC(O)$,

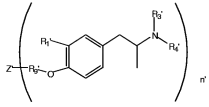
Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of the protein immunogenic carrier or the non-poly(amino acid) immunogenic carrier divided by about 500; and

(v) an antibody for methylenedioxyethamphetamine, the antibody being raised against a

compound of the formula (p 29, ln 26, to p 30, ln 10, and p 7, ln 29):



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is ethyl,

$R^{9'}$ is $-(CH_2)_nC(O)$,

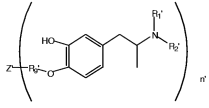
Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of the protein immunogenic carrier or the non-poly(amino acid) immunogenic carrier divided by about 500.

The medium is examined for the presence of a complex comprising the methylenedioxyamphetamine and the antibody for methylenedioxyamphetamine and a complex of the methylenedioxymethamphetamine and the antibody for methylenedioxymethamphetamine and a complex of the methylenedioxyethamphetamine and the antibody for methylenedioxyethamphetamine, the presence thereof indicating the presence of the methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in the sample (p 30, ln 11-18).

Claim 30 is directed to a kit comprising in packaged combination (p 34, ln 6): (i) an antibody for methylenedioxyamphetamine (p 34, ln 7), (ii) an antibody for methylenedioxymethamphetamine (p 34, ln 8), and/or (iii) an antibody for methylenedioxyethamphetamine (p 34, ln 9), and (iv) a compound of the formula (p 34, ln 10-19, and p 7, ln 29):



wherein:

$R^{1'}$ is H,

$R^{2'}$ is H, or methyl or ethyl,

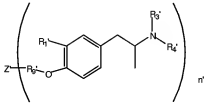
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is an enzyme,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said enzyme divided by about 500.

Claim 31 is directed to a kit comprising in packaged combination (p 34, ln 20): (i) a conjugate of an enzyme and a methylenedioxyamphetamine analog (p 34, ln 21-22) and/or a conjugate of an enzyme and a methylenedioxymethamphetamine analog (p 34, ln 23), and/or a conjugate of an enzyme and a methylenedioxyethamphetamine analog (p 34, ln 24), and (ii) an antibody for methylenedioxyamphetamine, said antibody being raised against a compound of the formula (p 34, ln 25, to p 35, ln 9, and p 7, ln 29):



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is H,

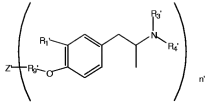
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500; and

(iii) an antibody for methylenedioxymethamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is methyl,

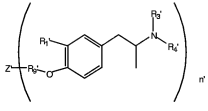
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500, and

(iv) an antibody for methylenedioxyethamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is ethyl,

$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier in or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following grounds of rejection are presented for review on appeal:

The rejection of Claims 25, 27, 30 and 31 under 35 U.S.C. §103(a) as unpatentable over Hui, *et al.* (EP 1,340,981 A2) (Hui) in view of Avenia, *et al.* (U.S. Patent No. 4,041,076) (Avenia).

The rejection of Claims 25, 27, 30 and 31 under 35 U.S.C. §103(a) as unpatentable over Rouhani, *et al.* (GB 2361473 A) (Rouhani) in view of Avenia.

ARGUMENT

The rejection of Claims 25, 27, 30 and 31 under 35 U.S.C. §103(a) as unpatentable over Hui in view of Avenia

Claims 25, 27, 30 and 31 were rejected (and the rejection made final) under paragraph (a) of 35 U.S.C. §103 as being unpatentable over Hui in view of Avenia. With regard to this rejection, Appellant submits that each of claims 25, 27, 30 and 31 are separately patentable over Hui in view of Avenia. The rejection of each of claims 25, 27, 30 and 31 as unpatentable over Hui in view of Avenia is separately discussed in the following sections of the Brief on Appeal.

The final rejection of claim 25 under 35 U.S.C. 103(a) as being unpatentable over Hui in view of Avenia

According to M.P.E.P. 2143.03, all claim limitations must be taught or suggested by the prior art in order to establish *prima facie* obviousness (citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Appellant's argument with regard to the rejection of claim 25 under the above code section may be summarized as follows. The combined teaching of Hui and Avenia is deficient in not disclosing or suggesting at least the following limitation of claim 25: "providing in combination in a medium, together with the sample and the antibodies, an enzyme label

conjugate of the formula set forth in the claim having a -$(CH_2)_nC(O)$ moiety linking the enzyme to the molecule."

The above limitation of claim 25 is not disclosed by the combined references

The combined teaching of Hui and Avenia is deficient in not disclosing the limitation of claim 25 that the combination in a medium comprises an enzyme label conjugate of the formula set forth in the claim having a -$(CH_2)_nC(O)$ moiety linking the enzyme to the molecule. Appellant submits that the Office recognizes this deficiency. There is nothing in the present record indicating that the combined references actually teach the above limitation.

The above limitation of claim 25 is not suggested by the combined references

Since the combined teaching of the references does not disclose the above limitation, the issue then becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. An objective analysis for applying 35 U.S.C. §103 is set forth in *Graham* v. *John Deere Co. of Kansas City*, 383 U. S. 1, 148 USPQ 459 (1966). The scope and content of the prior art are determined; differences between the prior art and the claims at issue are ascertained; and the level of ordinary skill in the pertinent art is resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Secondary considerations may also be evaluated. In determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, 810 F.2d 1561, 1 U.S.P.Q.2d 1593 (Fed Cir. 1987).

The scope and content of the prior art

Hui discloses compounds including haptens, intermediates, and immunogens that are useful in the production of antibodies specific for the methylenedioxy class of amphetamine derivatives. Antibodies specific for the methylenedioxy class of amphetamine derivatives, reagent kits containing antibodies specific for the methylenedioxy class of amphetamine derivatives, methods of producing antibodies specific for the methylenedioxy class of amphetamine derivatives, and methods of detecting analytes including members of the methylenedioxy class of amphetamine derivatives are also disclosed (Hui, Abstract).

Avenia discusses hapten compositions useful in preparing antigens that may be employed in eliciting antibodies useful in an improved radioimmunoassay for pharmacologically active

phenethylamines (Avenia, Abstract). Avenia discloses hapten conjugates as the antigens wherein a conventional immunogenic carrier (Avenia, col 2, ln 10-13) is linked to a phenylethylamine compound (Avenia, col 1, ln 38) by a $-(CH_2)_nC(O)$ moiety (Avenia, col 1, ln 56-63). The reference indicates that suitable labeled phenethylamines for assay purposes include radioisotopically labeled phenethylamines (Avenia, col 4, ln 47-48). The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide (col 10, ln 26-34).

There is no disclosure in Avenia of linking a phenylethylamine to a label by means of a $-(CH_2)_nC(O)$ moiety. Although Avenia states that enzymes may be suitable labels (Avenia, col 4, ln 57-58), it is only within the context of labeled phenethylamines as disclosed (Avenia, col 4, ln 47-58), namely, labeled derivatives that do not employ a $-(CH_2)_nC(O)$ linking moiety, which is only disclosed for Avenia's novel antigens for forming antibodies (Avenia, col 4, ln 59, to col 5, ln 10). Furthermore, Avenia states that his assays using the radiolabeled phenethylamine and the antibodies raised against his antigens having a $-(CH_2)_nC(O)$ moiety were clearly superior in all cases to assays utilizing free radical labels and enzyme labels (Avenia, col 11, ln 1-3, and col. 12, ln 1-3).

Differences between the prior art and claim 25

It appears undisputed that Hui individually does not disclose or suggest the limitation of claim 25 that the combination in a medium comprises an enzyme label conjugate of the formula set forth in the claim having a $-(CH_2)_nC(O)$ moiety linking the enzyme to the molecule. In addition, it appears clear that Avenia does not disclose the aforementioned limitation of claim 25. There is no mention in Avenia of a conjugate of a label and the haptens of the Avenia where the label is linked through a $-(CH_2)_nC(O)$ linking moiety. Moreover, there is no mention in Avenia of conjugates of enzymes and the haptens of the reference wherein a $-(CH_2)_nC(O)$ linking moiety is employed. This is consistent with the teaching of Avenia, who is concerned with conventional immunogenic carrier conjugates and not with label conjugates. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Furthermore, Avenia states that his assays using the reagents as disclosed were superior in all cases to assays utilizing free radical labels and enzyme labels.

The level of ordinary skill in the pertinent art

Based on the level of skill of the inventors in the present application and in the cited prior art, the level of ordinary skill in this art is an M.S. or Ph.D. in a biological science and at least 1 years of experience in the field of diagnostic assays or is a B.S. or a B.A. in a biological science and at least 5 years of experience in the field of diagnostic assays.

Non-obviousness of the subject matter of claim 25

As mentioned above, the issue becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.

The aforementioned limitation of claim 25 would not have been obvious to the skilled artisan in view of the combined teachings of Hui and Avenia. There is no mention in Avenia of conjugates of labels, including enzyme labels, and the haptens of the reference, which employ a -$(CH_2)_nC(O)$ linking moiety. This is consistent with the teaching of Avenia, who is concerned with conventional immunogenic carrier conjugates. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Furthermore, Avenia states that his assays using the above reagents were superior in all cases to assays utilizing free radical labels and enzyme labels. Accordingly, Avenia does not disclose or suggest the label conjugates used in the method of claim 25; and the reference, it may be argued, teaches away from such conjugates. This teaching away negates any motivation on the part of the skilled artisan to combine the teachings of Hui and Avenia in a manner to achieve the method of claim 25.

The Office responded to Appellant's argument by asserting that Avenia clearly envisaged using labeled phenethylamine in a competitive immunoassay using antibody against phenethylamine conjugate (referring to Avenia, column 4, lines 35-58). However, Appellant submits that it is clear from the cited paragraph that the reference is discussing labeled phenethylamine and not labeled haptens of the disclosure of Avenia, which employ a $(CH_2)_nC(O)$ linking moiety. The reference does not disclose or suggest using a -$(CH_2)_nC(O)$ linking moiety to conjugate haptens to a label. The only conjugates of the haptens of the reference that are disclosed in the reference are those of the haptens linked with a -$(CH_2)_nC(O)$ linking moiety to immunogenic carriers, not labels. This lack of disclosure or suggestion in the reference, when combined with Avenia's teaching that his assays using his reagents including a

radiolabeled phenethylamine were superior in all cases to assays utilizing free radical labels and enzyme labels, must negative any motivation that one skilled in the art might have to make the substitution as argued by the Office.

In the present situation there is no teaching or suggestion in Avenia to use label conjugates of his haptens in an assay method. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, 972 F. 2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992). Furthermore, as discussed above, according to M.P.E.P. 2143.03, all claim limitations must be taught or suggested by the prior art in order to establish *prima facie* obviousness (citing *In re Royka*, *supra*). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, *supra*. In the present situation, the combined teachings of the references do not render obvious the presently claimed method employing enzyme label conjugates having a $-(CH_2)_nC(O)$ linking moiety because not all the claim limitations are taught or suggested by the combined teachings.

The Office in the Advisory Action argues that Avenia discloses activated hapten (referring to formula III of Avenia) for conjugation of carrier protein to render the hapten immunogenic. Avenia, continues the Office, also discloses detection of phenethylamine in a sample using labeled phenethylamine, which competes with unknown phenethylamine in the sample in the detection process (referring to col 4, ln 35-44, of Avenia). The Office further asserts that Avenia discloses that suitable labeled phenethylamines for assay purposes include radioisotopically labeled phenethylamine and that Avenia discloses that other suitable labels include chromophores, fluorophores, enzymes, latex particle, etc., may be used (referring to col 4, ln 47-58, of Avenia). Therefore, argues the Office, Appellant's assertion that there is no teaching or suggestion in Avenia to use label conjugates is not persuasive because, even though Avenia describes assays using radiolabeled phenethylamines, Avenia suggests other non-radioactive label conjugates suitable for immunoassay detection. Since Avenia discloses activated haptens, one of ordinary skill in the art, argues the Office, would easily envision conjugating the label with the activated hapten.

Why would one skilled in the art do what the Office suggests? As discussed above, the assays of Avenia employing a radioactively labeled phenethylamine were clearly superior to assays employing enzyme labels and free radical labels. Why would one skilled in the art, in

view of this teaching of Avenia, invest the time in making enzyme label conjugates using the hapten of Avenia linking the label with a $-(CH_2)_nC(O)$ linking moiety when Avenia says the assays using radioactive label phenethylamine are clearly superior in all cases. In the present situation, the combined teachings of the references do not render obvious the presently claimed method employing enzyme label conjugates having a $-(CH_2)_nC(O)$ linking moiety.

The Office asserts that Avenia discloses activated hapten for conjugation to a carrier and also suggests label conjugates with fluorophores, enzymes and latex particle for use in competitive immunoassay and Hui discloses various competitive immunoassay formats for quantitative detection of amphetamine derivatives using antibody against amphetamine (phenethylamine) derivatives and label conjugates. Therefore, concludes the Office, since antibody and labeled conjugates are disclosed for phenethylamine, one of ordinary skill in the art would obviously try different immunoassay formats as taught by Hui to develop a better detection assay for the drug because Hui is also concerned with the immunodetection of phenethylamine in a sample.

Appellant reiterates the above question, namely, in view of the teaching of Avenia that assays using radioactively labeled phenethylamine are clearly superior in all cases, why would one skilled in the art invest the time, effort and expense in making enzyme label conjugates using the hapten of Avenia linking the label with a $-(CH_2)_nC(O)$ linking moiety? The reference does not teach that use of enzyme labels results in a better detection assay. Avenia teaches just the opposite. The Office has attempted to piece together portions of the references in an effort to produce the presently claimed method. The Office is required to consider all that a reference discloses; piecemeal reconstruction of the prior art is not allowed. It is not permissible to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. *In re Wesslan*, 147 USPQ 391, 827 O.G. 348 (1966). In the present situation, the combined teachings of the references do not render obvious the presently claimed method employing enzyme label conjugates having a $-(CH_2)_nC(O)$ linking moiety because the combined teachings do not fairly suggest the present method to one of ordinary skill in the art.

The final rejection of claim 27 under 35 U.S.C. 103(a) as being unpatentable over Hui in view of Avenia

Appellant's argument with regard to the rejection of claim 27 under the above code section may be summarized as follows. The combined teaching of Hui and Avenia is deficient in not disclosing or suggesting at least the following limitation of the method of claim 27: "providing in combination in a medium, together with the sample and the antibodies, an enzyme label conjugate of a methylenedioxyamphetamine analog and an enzyme label conjugate of a methylenedioxymethamphetamine analog and an enzyme label conjugate of a methylenedioxyethamphetamine analog."

The above limitation of claim 27 is not disclosed by the combined references

The combined teaching of Hui and Avenia is deficient in not disclosing the limitation of claim 27 that the combination in a medium comprises an enzyme label conjugate for each of methylenedioxyamphetamine, methylenedioxymethamphetamine and methylenedioxy-ethamphetamine. Appellant submits that the Office recognizes this deficiency. There is nothing in the present record indicating that the combined references actually teach the above limitation.

The above limitation of claim 27 is not suggested by the combined references

Since the combined teaching of the references does not disclose the above limitation, the issue then becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. As mentioned above, an objective analysis for applying 35 U.S.C. §103 is set forth in *Graham* v. *John Deere Co. of Kansas City*, *supra*.

The scope and content of the prior art

The scope and content of the prior art are set forth above.

Differences between the prior art and claim 27

It appears undisputed that Hui individually does not disclose or suggest the limitation of claim 27 that the combination in a medium comprises antibodies raised against an immunogenic conjugate of the formula set forth in the claim having a $-(CH_2)_nC(O)$ moiety linking the immunogenic carrier to the molecule. In addition, Avenia teaches away from using enzyme label conjugates in assays. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-

methylphenethylamine hydrobromide. As mentioned above, Avenia states that his assays using the reagents as disclosed were superior in all cases to assays utilizing free radical labels and enzyme labels.

The level of ordinary skill in the pertinent art

The level of ordinary skill in the pertinent art is set forth above.

Non-obviousness of the subject matter of claim 27

As mentioned above, the issue becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.

The aforementioned limitation of claim 27 would not have been obvious to the skilled artisan in view of the combined teachings of Hui and Avenia. The labeled derivative that Avenia recommends for his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Avenia states that his assays using the above reagents were superior in all cases to assays utilizing free radical labels and enzyme labels. Accordingly, Avenia does not disclose or suggest the use of enzyme label conjugates; and the reference, it may be argued, teaches away from such conjugates. This teaching away negates any motivation on the part of the skilled artisan to combine the teachings of Hui and Avenia in a manner as asserted by the Office to achieve the method of claim 27. As mentioned above, in determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, *supra*.

In the present situation there is no teaching or suggestion in Avenia to use enzyme label conjugates in an assay method. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, *supra*. Furthermore, as discussed above, according to M.P.E.P. 2143.03, all claim limitations must be taught or suggested by the prior art in order to establish *prima facie* obviousness (citing *In re Royka*, *supra*). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, *supra*. In the present situation, the combined teachings of the references do not render obvious the presently claimed method employing enzyme label conjugates having a $-(CH_2)_nC(O)$ linking moiety.

Why would one skilled in the art do what the Office suggests? As discussed above, the

assays of Avenia employing a radioactively labeled phenethylamine were clearly superior to assays employing enzyme labels and free radical label. Why would one skilled in the art, in view of this teaching of Avenia, use enzyme label conjugates when Avenia says the assays using radioactive label phenethylamine are clearly superior in all cases. In the present situation, the combined teachings of the references do not render obvious the presently claimed method employing enzyme label conjugates. The Office has attempted to piece together portions of the references in an effort to produce the presently claimed kit. The Office is required to consider all that a reference discloses; piecemeal reconstruction of the prior art is not allowed. It is not permissible to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. *In re Wesslan*, *supra*.

The Office asserts that Avenia discloses activated hapten for conjugation to a carrier and also suggests label conjugates with fluorophores, enzymes and latex particle for use in competitive immunoassay and Hui discloses various competitive immunoassay formats for quantitative detection of amphetamine derivatives using antibody against amphetamine (phenethylamine) derivatives and label conjugates. Therefore, concludes the Office, since antibody and labeled conjugates are disclosed for phenethylamine, one of ordinary skill in the art would obviously try different immunoassay formats as taught by Hui to develop a better detection assay for the drug because Hui is also concerned with the immunodetection of phenethylamine in a sample.

Appellant reiterates the above question, namely, in view of the teaching of Avenia that assays using radioactively labeled phenethylamine are clearly superior in all cases, why would one skilled in the art invest the time, effort and expense in making and using enzyme label conjugates in the method of Avenia when the reference teaches away from using enzyme label conjugates? The reference does not teach that use of enzyme labels results in a better detection assay. Rather, the reference teaches just the opposite. As mentioned above, in determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, *supra*.

The final rejection of claim 30 under 35 U.S.C. 103(a) as being unpatentable over Hui in view of Avenia

Appellant's argument with regard to the rejection of claim 30 under the above code section may be summarized as follows. The combined teaching of Hui and Avenia is deficient in not disclosing or suggesting at least the following limitation of claim 30: "providing in packaged combination together with the antibodies, an enzyme label conjugate of the formula set forth in the claim having a $-(CH_2)_nC(O)$ moiety linking the enzyme to the molecule."

The above limitation of claim 30 is not disclosed by the combined references

The combined teaching of Hui and Avenia is deficient in not disclosing the limitation of claim 30 that the packaged combination comprises an enzyme label conjugate of the formula set forth in the claim having a $-(CH_2)_nC(O)$ moiety linking the enzyme to the molecule. Appellant submits that the Office recognizes this deficiency. There is nothing in the present record indicating that the combined references actually teach the above limitation.

The above limitation of claim 30 is not suggested by the combined references

Since the combined teaching of the references does not disclose the above limitation, the issue then becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. As mentioned above, an objective analysis for applying 35 U.S.C. §103 is set forth in *Graham* v. *John Deere Co. of Kansas City*, *supra*.

The scope and content of the prior art

The scope and content of the prior art are set forth above.

Differences between the prior art and claim 30

It appears undisputed that Hui individually does not disclose or suggest the limitation of claim 30 that the packaged combination comprises an enzyme label conjugate of the formula set forth in the claim having a $-(CH_2)_nC(O)$ moiety linking the enzyme to the molecule. In addition, it appears clear that Avenia does not disclose the aforementioned limitation of claim 30. There is no mention in Avenia of a conjugate of a label and the haptens of the Avenia where the label is linked through a $-(CH_2)_nC(O)$ linking moiety. Moreover, there is no mention in Avenia of conjugates of enzymes and the haptens of the reference wherein a $-(CH_2)_nC(O)$ linking moiety is employed. This is consistent with the teaching of Avenia, who is concerned with conventional

immunogenic carrier conjugates and not with label conjugates. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Furthermore, Avenia states that his assays using the reagents as disclosed were superior in all cases to assays utilizing free radical labels and enzyme labels.

The level of ordinary skill in the pertinent art

The level of ordinary skill in the pertinent art is set forth above.

Non-obviousness of the subject matter of claim 30

As mentioned above, the issue becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.

The aforementioned limitation of claim 30 would not have been obvious to the skilled artisan in view of the combined teachings of Hui and Avenia. There is no mention in Avenia of conjugates of labels, including enzyme labels, and the haptens of the reference, which employ a -$(CH_2)_nC(O)$ linking moiety. This is consistent with the teaching of Avenia, who is concerned with conventional immunogenic carrier conjugates. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Furthermore, Avenia states that his assays using the above reagents were superior in all cases to assays utilizing free radical labels and enzyme labels. Accordingly, Avenia does not disclose or suggest the label conjugates used in the method of claim 30; and the reference, it may be argued, teaches away from such conjugates. This teaching away negates any motivation on the part of the skilled artisan to combine the teachings of Hui and Avenia in a manner to achieve the method of claim 30. As mentioned above, in determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, *supra*.

The Office responded to Appellant's argument by asserting that Avenia clearly envisaged using labeled phenethylamine in a competitive immunoassay using antibody against phenethylamine conjugate (referring to Avenia, column 4, lines 35-58). However, Appellant submits that it is clear from the cited paragraph that the reference is discussing labeled phenethylamine and not labeled haptens of the disclosure of Avenia, which employ a

$(CH_2)_nC(O)$ linking moiety. The reference does not disclose or suggest using a $-(CH_2)_nC(O)$ linking moiety to conjugate haptens to a label. The only conjugates of the haptens of the reference that are disclosed in the reference are those of the haptens linked with a $-(CH_2)_nC(O)$ linking moiety to immunogenic carriers, not labels. This lack of disclosure or suggestion in the reference, when combined with Avenia's teaching that his assays using his reagents including a radiolabeled phenethylamine were superior in all cases to assays utilizing free radical labels and enzyme labels, must negative any motivation that one skilled in the art might have to make the substitution as argued by the Office.

In the present situation there is no teaching or suggestion in Avenia to use label conjugates of his haptens in an assay method. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, *supra*. Furthermore, as discussed above, according to M.P.E.P. 2143.03, all claim limitations must be taught or suggested by the prior art in order to establish *prima facie* obviousness (citing *In re Royka*, *supra*). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, *supra*. In the present situation, the combined teachings of the references do not render obvious the presently claimed kit that comprises enzyme label conjugates having a $-(CH_2)_nC(O)$ linking moiety.

The Office in the Advisory Action argues that Avenia discloses activated hapten (referring to formula III of Avenia) for conjugation of carrier protein to render the hapten immunogenic. Avenia, continues the Office, also discloses detection of phenethylamine in a sample using labeled phenethylamine, which competes with unknown phenethylamine in the sample in the detection process (referring to col 4, ln 35-44, of Avenia). The Office further asserts that Avenia discloses that suitable labeled phenethylamines for assay purposes include radioisotopically labeled phenethylamine and that Avenia discloses that other suitable labels include chromophores, fluorophores, enzymes, latex particle, etc., may be used (referring to col 4, ln 47-58, of Avenia). Therefore, argues the Office, Appellant's assertion that there is no teaching or suggestion in Avenia to use label conjugates is not persuasive because, even though Avenia describes assays using radiolabeled phenethylamines, Avenia suggests other non-radioactive label conjugates suitable for immunoassay detection. Since Avenia discloses activated haptens, one of ordinary skill in the art, argues the Office, would easily envision

conjugating the label with the activated hapten.

Why would one skilled in the art do what the Office suggests? As discussed above, the assays of Avenia employing a radioactively labeled phenethylamine were clearly superior to assays employing enzyme labels and free radical labels. Why would one skilled in the art, in view of this teaching of Avenia, invest the time in making enzyme label conjugates using the hapten of Avenia linking the label with a $-(CH_2)_nC(O)$ linking moiety when Avenia says the assays using radioactive label phenethylamine are clearly superior in all cases. As mentioned above, in determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, *supra*. In the present situation, the combined teachings of the references do not render obvious the presently claimed kit that comprises enzyme label conjugates having a $(CH_2)_nC(O)$ linking moiety.

The Office asserts that Avenia discloses activated hapten for conjugation to a carrier and also suggests label conjugates with fluorophores, enzymes and latex particle for use in competitive immunoassay and Hui discloses various competitive immunoassay formats for quantitative detection of amphetamine derivatives using antibody against amphetamine (phenethylamine) derivatives and label conjugates. Therefore, concludes the Office, since antibody and labeled conjugates are disclosed for phenethylamine, one of ordinary skill in the art would obviously try different immunoassay formats as taught by Hui to develop a better detection assay for the drug because Hui is also concerned with the immunodetection of phenethylamine in a sample.

Appellant reiterates the above question, namely, in view of the teaching of Avenia that assays using radioactively labeled phenethylamine are clearly superior in all cases, why would one skilled in the art invest the time, effort and expense in making enzyme label conjugates using the hapten of Avenia linking the label with a $-(CH_2)_nC(O)$ linking moiety? The reference does not teach that use of enzyme labels results in a better detection assay. Rather, the Avenia reference teaches just the opposite. The Office has attempted to piece together portions of the references in an effort to produce the presently claimed method. The Office is required to consider all that a reference discloses; piecemeal reconstruction of the prior art is not allowed. It is not permissible to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such

reference fairly suggests to one of ordinary skill in the art. *In re Wesslan*, *supra*. In the present situation, the combined teachings of the references do not render obvious the presently claimed kit comprising enzyme label conjugates having a $-(CH_2)_nC(O)$ linking moiety because such enzyme label conjugates are not fairly suggested to the skilled artisan.

The final rejection of claim 31 under 35 U.S.C. 103(a) as being unpatentable over Hui in view of Avenia

Appellant's argument with regard to the rejection of claim 31 under the above code section may be summarized as follows. The combined teaching of Hui and Avenia is deficient in not disclosing or suggesting at least the following limitation of the method of claim 31: "providing in packaged combination, together with the antibodies, an enzyme label conjugate of a methylenedioxyamphetamine analog and an enzyme label conjugate of a methylenedioxy-methamphetamine analog and an enzyme label conjugate of a methylenedioxyethamphetamine analog."

The above limitation of claim 31 is not disclosed by the combined references

The combined teaching of Hui and Avenia is deficient in not disclosing the limitation of claim 31 that the combination comprises an enzyme label conjugate for each of methylenedioxyamphetamine, methylenedioxymethamphetamine and methylenedioxy-ethamphetamine. Appellant submits that the Office recognizes this deficiency. There is nothing in the present record indicating that the combined references actually teach the above limitation.

The above limitation of claim 31 is not suggested by the combined references

Since the combined teaching of the references does not disclose the above limitation, the issue then becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. As mentioned above, an objective analysis for applying 35 U.S.C. §103 is set forth in *Graham* v. *John Deere Co. of Kansas City*, *supra*.

The scope and content of the prior art

The scope and content of the prior art are set forth above.

Differences between the prior art and claim 31

It appears undisputed that Hui individually does not disclose or suggest the limitation of

claim 31 that the packaged combination comprises antibodies raised against an immunogenic conjugate of the formula set forth in the claim having a $-(CH_2)_nC(O)$ moiety linking the immunogenic carrier to the molecule. In addition, Avenia teaches away from using enzyme label conjugates in assays. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. As mentioned above, Avenia states that his assays using the reagents as disclosed were superior in all cases to assays utilizing free radical labels and enzyme labels.

The level of ordinary skill in the pertinent art

The level of ordinary skill in the pertinent art is set forth above.

Non-obviousness of the subject matter of claim 31

As mentioned above, the issue becomes whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.

The aforementioned limitation of claim 31 would not have been obvious to the skilled artisan in view of the combined teachings of Hui and Avenia. The labeled derivative that Avenia recommends for his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Avenia states that his assays using the above reagents were superior in all cases to assays utilizing free radical labels and enzyme labels. Accordingly, Avenia does not disclose or suggest the use of enzyme label conjugates; and the reference, it may be argued, teaches away from such conjugates. This teaching away negates any motivation on the part of the skilled artisan to combine the teachings of Hui and Avenia in a manner as asserted by the Office to achieve the kit of claim 31. As mentioned above, in determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, *supra*.

In the present situation there is no teaching or suggestion in Avenia to use enzyme label conjugates in an assay method. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, *supra*. Furthermore, as discussed above, according to M.P.E.P. 2143.03, all claim limitations must be taught or suggested by the prior art in order to establish

prima facie obviousness (citing *In re Royka, supra*). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson, supra.* In the present situation, the combined teachings of the references do not render obvious the presently claimed kit comprising enzyme label conjugates having a $-(CH_2)_nC(O)$ linking moiety.

Why would one skilled in the art do what the Office suggests? As discussed above, the assays of Avenia employing a radioactively labeled phenethylamine were clearly superior to assays employing enzyme labels and free radical label. Why would one skilled in the art, in view of this teaching of Avenia, use enzyme label conjugates when Avenia says the assays using radioactive label phenethylamine are clearly superior in all cases? The Office has attempted to piece together portions of the references in an effort to produce the presently claimed kit. The Office is required to consider all that a reference discloses; piecemeal reconstruction of the prior art is not allowed. It is not permissible to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. *In re Wesslan, supra.* In the present situation, the combined teachings of the references do not render obvious the presently claimed kit comprising enzyme label conjugates because the combined teachings do not disclose or suggest such enzyme label conjugates.

The Office asserts that Avenia discloses activated hapten for conjugation to a carrier and also suggests label conjugates with fluorophores, enzymes and latex particle for use in competitive immunoassay and Hui discloses various competitive immunoassay formats for quantitative detection of amphetamine derivatives using antibody against amphetamine (phenethylamine) derivatives and label conjugates. Therefore, concludes the Office, since antibody and labeled conjugates are disclosed for phenethylamine, one of ordinary skill in the art would obviously try different immunoassay formats as taught by Hui to develop a better detection assay for the drug because Hui is also concerned with the immunodetection of phenethylamine in a sample.

Appellant reiterates the above question, namely, in view of the teaching of Avenia that assays using radioactively labeled phenethylamine are clearly superior in all cases, why would one skilled in the art invest the time, effort and expense in making and using enzyme label conjugates in the method of Avenia when the reference teaches away from using enzyme label conjugates? As mentioned above, in determining the scope and content of the prior art,

references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit, supra.*

The rejection of Claims 25, 27, 30 and 31 under 35 U.S.C. §103(a) as unpatentable over Rouhani in view of Avenia

Claims 25, 27, 30 and 31 were rejected (and the rejection made final) under paragraph (a) of 35 U.S.C. §103 as being unpatentable over Rouhani in view of Avenia. With regard to this rejection, Appellant submits that each of claims 25, 27, 30 and 31 are separately patentable over Rouhani in view of Avenia for reasons similar to those set forth above with regard to the rejection of each of claims 25, 27, 30 and 31 as unpatentable over Hui in view of Avenia. Accordingly, for the sake of brevity, these arguments will not be repeated here.

CONCLUSION AND RELIEF SOUGHT

Appellant has demonstrated above that claim 25 is separately patentable over Hui in view of Avenia and over Rouhani in view of Avenia. Even if for the sake of argument the teachings of the references were combined, the combination of teachings is deficient in not disclosing or suggesting each and every element of the claim. The combination of teachings fails to disclose or suggest the limitation of claim 25, which recites providing in combination in a medium, together with the sample and the antibodies, an enzyme label conjugate of the formula set forth in the claim having a $-(CH_2)_nC(O)$ moiety linking the enzyme to the molecule.

Appellant has demonstrated above that claim 27 is separately patentable over Hui in view of Avenia and over Rouhani in view of Avenia. Even if for the sake of argument the teachings of the references were combined, the combination of teachings is deficient in not disclosing or suggesting each and every element of the claim. The combination of teachings fails to disclose or suggest the limitation of claim 27 that the combination in a medium comprises an enzyme label conjugate for each of methylenedioxyamphetamine, methylenedioxymethamphetamine and methylenedioxy-ethamphetamine.

Appellant has demonstrated above that claim 30 is separately patentable over Hui in view of Avenia and over Rouhani in view of Avenia. Even if for the sake of argument the teachings of the references were combined, the combination of teachings is deficient in not disclosing or

suggesting each and every element of the claim. The combination of teachings fails to disclose or suggest the limitation of claim 30, which recites providing in packaged combination, together with the antibodies, an enzyme label conjugate of the formula set forth in the claim having a $(CH_2)_nC(O)$ moiety linking the enzyme to the molecule.

Appellant has demonstrated above that claim 31 is separately patentable over Hui in view of Avenia and over Rouhani in view of Avenia. Even if for the sake of argument the teachings of the references were combined, the combination of teachings is deficient in not disclosing or suggesting each and every element of the claim. The combination of teachings fails to disclose or suggest the limitation of claim 31 that the packaged combination comprises an enzyme label conjugate for each of methylenedioxyamphetamine, methylenedioxymethamphetamine and methylenedioxy-ethamphetamine.

Accordingly, Appellant respectfully requests that the Board of Patent Appeals and Interferences reverse the following objections and rejections:

(a) the separate rejections under 35 U.S.C. 103(a) of claims 25, 27, 30 and 31, respectively as being unpatentable over Hui in view of Avenia and

(b) the separate rejections under 35 U.S.C. 103(a) of claims 25, 27, 30 and 31, respectively as being unpatentable over Rouhani in view of Avenia.

Respectfully submitted,

/Theodore J. Leitereg/

Theodore J. Leitereg, Reg. No. 28,319
Attorney for Appellant

Theodore J. Leitereg
31420 Pennant Ct.
Temecula CA 92591
(602) 369-1751

CLAIMS APPENDIX

25. A method for determining methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in a sample suspected of containing methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine, said method comprising:

(a) providing in combination in a medium:

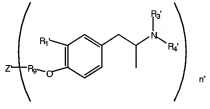
(i) said sample,

(ii) an antibody for methylenedioxyamphetamine, and/or

(iii) an antibody for methylenedioxymethamphetamine, and/or

(iv) an antibody for methylenedioxyethamphetamine, and

(v) a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is H, or methyl or ethyl,

R^9 is $-(CH_2)_nC(O)$,

Z' is an enzyme,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said enzyme divided by about 500; and

(b) examining said medium for the presence of a complex comprising said methylenedioxyamphetamine and said antibody for methylenedioxyamphetamine and/or a complex of said methylenedioxymethamphetamine and said antibody for methylenedioxymethamphetamine and/or a complex of said methylenedioxyethamphetamine and said antibody for methylenedioxyethamphetamine, the presence thereof indicating the presence of said methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or

methylenedioxyethamphetamine in said sample.

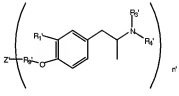
27. A method for determining methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in a sample suspected of containing methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine, said method comprising:

(a) providing in combination in a medium:

(i) said sample,

(ii) a conjugate of an enzyme and a methylenedioxyamphetamine analog and a conjugate of an enzyme and a methylenedioxymethamphetamine analog and a conjugate of an enzyme and a methylenedioxyethamphetamine analog,

(iii) an antibody for methylenedioxyamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is H,

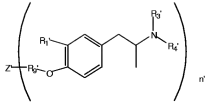
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500; and

(iv) an antibody for methylenedioxymethamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is methyl,

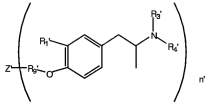
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500; and

(v) an antibody for methylenedioxyethamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is ethyl,

$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500; and

(b) examining said medium for the presence of a complex comprising said methylenedioxyamphetamine and said antibody for methylenedioxyamphetamine and a complex of said methylenedioxymethamphetamine and said antibody for

methylenedioxymethamphetamine and a complex of said methylenedioxyethamphetamine and said antibody for methylenedioxyethamphetamine, the presence thereof indicating the presence of said methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in said sample.

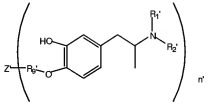
30. A kit comprising in packaged combination:

(i) an antibody for methylenedioxyamphetamine,

(ii) an antibody for methylenedioxymethamphetamine, and/or

(iii) an antibody for methylenedioxyethamphetamine, and

(iv) a compound of the formula:



wherein:

$R^{1'}$ is H,

$R^{2'}$ is H, or methyl or ethyl,

$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is an enzyme,

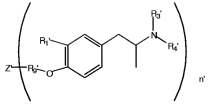
n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said enzyme divided by about 500.

31. A kit comprising in packaged combination:

(i) a conjugate of an enzyme and a methylenedioxyamphetamine analog and/or a conjugate of an enzyme and a methylenedioxymethamphetamine analog, and/or a conjugate of an enzyme and a methylenedioxyethamphetamine analog, and

(ii) an antibody for methylenedioxyamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is H,

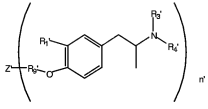
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500; and

(iii) an antibody for methylenedioxymethamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is methyl,

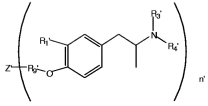
$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500, and

(iv) an antibody for methylenedioxyethamphetamine, said antibody being raised against a compound of the formula:



wherein:

$R^{1'}$ is H, or methyl or ethyl

$R^{3'}$ is H,

$R^{4'}$ is ethyl,

$R^{9'}$ is $-(CH_2)_nC(O)$,

Z' is a protein immunogenic carrier in or a non-poly(amino acid) immunogenic carrier,

n is an integer from 1 to 5,

n' is an integer between 1 and the molecular weight of said protein immunogenic carrier or said non-poly(amino acid) immunogenic carrier divided by about 500.

EVIDENCE APPENDIX

No additional evidence is submitted.

RELATED PROCEEDINGS APPENDIX

There are no related proceedings.